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RNase1 prevents the damaging interplay between extracellular RNA and tumour necrosis factor-α in cardiac ischaemia/reperfusion injury

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Abstract

© Schattauer 2014 Despite optimal therapy, the morbidity and mortality of patients presenting with an acute myocardial infarction (M1) remain significant, and the initial mechanistic trigger of myocardial “ischaemia/reperfusion (1/R) injury” remains greatly unexplained. Here we show that factors released from the damaged cardiac tissue itself, in particular extracellular RNA (eRNA) and tumour-necrosis-factor α (TNF-α), may dictate 1/R injury. In an experimental in vivo mouse model of myocardial 1/R as well as in the isolated 1/R Langendorff-perfused rat heart, cardiomyocyte death was induced by eRNA and TNF-α. Moreover, TNF-α promoted further eRNA release especially under hypoxia, feeding a vicious cell damaging cycle during 1/R with the massive production of oxygen radicals, mitochondrial obstruction, decrease in antioxidant enzymes and decline of cardiomyocyte functions. The administration of RNase1 significantly decreased myocardial infarction in both experimental models. This regimen allowed the reduction in cytokine release, normalisation of antioxidant enzymes as well as preservation of cardiac tissue. Thus, RNase1 administration provides a novel therapeutic regimen to interfere with the adverse eRNA-TNF-α interplay and significantly reduces or prevents the pathological outcome of ischaemic heart disease.

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Keywords

Cardiology, Cytokines, Inflammatory mediators, Ischaemic heart disease